



STUDY OF INFLAMMATORY MARKERS IN RELATION TO RADIOLOGICAL FINDINGS IN COVID 19

Respiratory Medicine

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ABSTRACT

BACKGROUND Currently, the Coronavirus disease 2019 (COVID-19) has become pandemic globally. Elevated inflammatory markers are observed and are a common pathophysiological response to acute illness. Chest X-ray changes are also commonly seen in COVID-19 patients. The present study was undertaken to determine the relationship between inflammatory markers to chest X-ray findings in COVID-19 patients.

METHODS This is a prospective observational study of COVID-19 patients admitted to tertiary care hospital from May 2020-November 2020. Comorbidities, inflammatory markers, and Chest X-ray were collected and analyzed. Correlations between radiological and inflammatory markers were studied.

AIMS & OBJECTIVES:

- Correlation of inflammatory markers to radiographic findings and their outcome in COVID 19 patients
- The outcome was studied in terms of:
- Patients requiring oxygen/NIV support
- duration of hospital stay
- Number of patients Recovered/death

RESULTS:

- Out of 500 patients studied, the mean age was 49.41 years, and (295)59% of patients were male, (205)41% were females. (455)91% patients discharged and (43)8.6% died. We found a positive correlation between inflammatory markers and Chest X-ray findings at the time of admission with a significant statistical P-value. The inflammatory markers CRP, ESR, D-Dimer & Sr.ferritin compared with the mode of ventilation (O2 & NIV, duration of hospital stay and outcome also showed significant statistical P-value.

CONCLUSIONS

We conclude that in patients with raised inflammatory markers there were increased abnormalities on Chest X-rays which required an increase in oxygen or NIV support. This can be a useful predictor of the severity of the disease and assessment of outcome.

KEYWORDS

COVID-19; CHEST X-RAY; inflammatory markers.

INTRODUCTION:

The rapid outbreak of coronavirus disease 2019 (COVID-19) which emerged in Wuhan, China at the end of 2019, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread across the globe. As the numbers of infected and fatal cases have dramatically increased throughout the world, it is a key role to reveal the radiological and laboratory characteristics, in severe COVID-19 patients.(1)

Accumulating evidence has suggested that inflammatory responses play a critical role in the progression of COVID-19(2,3). Inflammatory responses triggered by rapid viral replication of SARS-CoV-2 and cellular destruction can recruit macrophages and monocytes and induce the release of cytokines and chemokines(4). These cytokines and chemokines then attracted immune cells and activated immune responses, leading to cytokine storm and aggravation(5). Cytokine storm syndrome is a diverse set of conditions of pleiotropic causation associated with exuberant systemic inflammation, multi-organ failure, hyperferritinemia, and high mortality(6)

Several inflammatory markers have some tracing and detecting accuracy for disease severity and fatality(7). Inflammatory markers such as procalcitonin (PCT), serum ferritin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and interleukin-6 (IL-6) have been reported to be significantly associated with the high-risks of the development of severe COVID-19(8,9,10).

It was found that higher levels of C-reactive proteins (CRP), D-dimer, ESR, Sr ferritin were seen in severe patients when compared to non-severe patients.(11) Elderly age, presence of comorbidities & high levels of D-dimer, ESR, Sr. ferritin, were reported to be the risk factors associated with mortality in severe patients.(12-15)

CRP is a clinically wide used inflammatory marker. (16). High levels of CRP indicate inflammation caused by various conditions including infections(16). ESR is a non-specific inflammatory marker that mainly reflects the change of plasma protein(17,18).

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METHODOLOGY:

Institutional ethical clearance was taken. This is a Prospective observational study conducted in DR.PSIMS & RF hospital for over a period of 6 months (MAY 2020-NOV 2020). 500 COVID-19 Patients were included in the study, age more than 18 years.

Patients aged less than 18 years, known cases of vascular diseases, any recent episodes of myocardial infarction were excluded from the study.

Inflammatory markers like CRP, D-DIMER, Sr ferritin, ESR, & CXR PA View findings were obtained.

To quantify the extent of infection a severity score was calculated by adapting and simplifying the Radiographic Assessment of Lung Edema (RALE) score proposed by the British Society of Thoracic Imaging (BSTI). Mild disease means 0-25% lung abnormality, moderate means >25-50% and severe >50%.(19,20).

RESULTS:**Table: 1 Correlation of inflammatory markers with Chest X-ray**

Inflammatory markers	XRAY	N	Mean ± SD	F value	P value
ESR	Normal	270	20.89 ± 13.79	5.35	0.001
	Mild	83	22.45 ± 15.63		
	Moderate	87	26.49 ± 18.29		
	Severe	60	27.88 ± 16.31		
CRP	Normal	270	13.66 ± 25.58	28.98	<0.0001
	Mild	83	13.95 ± 15.46		
	Moderate	87	26.45 ± 29.74		
	Severe	60	47.02 ± 36.36		
D-Dimer	Normal	270	213.89±181.77	42.85	<0.0001
	Mild	83	233.26±124.88		
	Moderate	87	275.1±212.59		
	Severe	60	596.36±492.32		
Serum Ferritin	Normal	270	155.97±208.40	42.54	<0.0001
	Mild	83	197.76±210.19		
	Moderate	87	284.56±285.87		
	Severe	60	584.39±486.4		

Table 2: Correlation of inflammatory markers with the mode of ventilation

Inflammatory markers	Mode Of Ventilation	N	Mean ± SD	F value	P-value
ESR	RA	394	21.79 ± 14.56	6.88	0.001
	NIV	75	28.94 ± 18.98		
	Oxygen	31	23.19 ± 14.27		
CRP	RA	394	15.01 ± 24.28	34.79	<0.001
	NIV	75	42.79 ± 37.21		
	Oxygen	31	27.39 ± 29.64		
D-Dimer	RA	394	212.73±168.96	72.39	<0.001
	NIV	75	565.49±445.91		
	Oxygen	31	349.14±239.07		
Serum Ferritin	RA	394	212.16±211.72	86.72	<0.001
	NIV	75	592.37±435.92		
	Oxygen	31	312.57±267.53		

Table: 3 Association of inflammatory markers with the outcome

Inflammatory markers	Outcome	N	Mean ± SD	T value	P-value
ESR	Recovered	457	22.15 ± 14.69	-3.83	0.005
	Death	43	31.45 ± 20.43		
CRP	Recovered	457	16.85 ± 25.03	-8.15	<0.0001
	Death	43	51.89 ± 42.49		
D-Dimer	Recovered	457	236.91±197.89	-10.89	<0.0001
	Death	43	656.49±515.13		
Serum Ferritin	Recovered	457	193.03±237	-12.09	<0.0001
	Death	43	707.25±481.78		

Table 4: Association of inflammatory markers with days of hospital stay

Inflammatory markers	Days of Stay in hospital	N	Mean ± SD	t value	P-value
ESR	≤7	149	25.28 ± 16.71	2.22	0.02
	>7	348	21.79 ± 14.55		
CRP	≤7	149	30.02 ± 33.68	4.84	<0.0001
	>7	348	15.19 ± 24.67		
D-Dimer	≤7	149	392.93±366.68	5.53	<0.0001
	>7	348	218.43±181.37		
Serum Ferritin	≤7	149	307.72±378.59	5.93	<0.0001
	>7	348	173.1±227.21		

DISCUSSION:

500 COVID 19 patients were included in this study. The mean age of patients is 49.41. Males constitute (295)59% and (205)41% were females. Males are more affected than females. A similar study On Covid conducted by Chen et al Huang et al, Wang et al., also showed male preponderance (21,22,23).

In table 1 by comparing the mean and standard deviation (SD) of inflammatory markers CRP(C reactive protein), ESR, D dimer, Serum

Ferritin with chest x-ray findings by using ANOVA test which is classified as mild, moderate, severe at the time of presentation there is statistically high significant relation of CRP, ESR, D- Dimer & Sr.ferritin to Chest X-ray with P-value of < 0.0001,0.001, <0.0001 & <0.0001 respectively. Of this CRP is the most sensitive inflammatory marker. This suggests that a higher inflammatory marker is associated with more severe Chest X-ray changes.

Similar findings were reported by Sarfraz Saleemi et al, which showed severe radiographic findings, associated with elevated inflammatory markers(24).

A study conducted by Wu et al., also showed elevated high-sensitivity C-reactive protein (hs-CRP) was significantly associated with higher risks of acute respiratory distress syndrome (ARDS) in COVID-19 patients(16)

In table 2 by comparing the mean and standard deviation (SD) of inflammatory markers ESR, CRP(C reactive protein),D dimer, Serum Ferritin to the mode of ventilation using ANOVA test there is a statistically high significant relation of CRP, ESR, D- Dimer & Sr.ferritin to MOV (O2 & NIV) with P-value of <0.001,0.001, <0.001 & <0.001 respectively. This suggests that the patients with higher level of inflammatory markers required either oxygen or NIV support.

Similar findings were reported by Tobias Herold MD et al., which showed maximal CRP levels had the strongest association with O2 or noninvasive mechanical ventilation. (25)

In Tables 3 and 4 by comparing the mean & SD of inflammatory markers ESR, CRP, D-Dimer, & Serum ferritin the outcome and duration of hospital stay by using the independent test, there is high significance statistically.

Similar findings were reported by Zhilin Zeng et al., showed higher inflammatory markers like high sensitivity C- reactive protein had the strongest association with outcome and duration of hospital stay(26) Patients with higher inflammatory markers had high morbidity and mortality.

CONCLUSION:

- Higher the inflammatory markers, the more severe the radiographic(CXR) findings.
- Inflammatory markers and CXR are cost-effective & can be used as disease severity markers.
- These early & effective predictors can be used for better risk stratification, monitoring & timely intervention.

LIMITATIONS:

- Correlation with Inflammatory marker IL-6 could not be done.

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